WHAT IS CLAIMED IS

1. A method of designing a humanized immunoglobulin (Ig) chain having a framework region from a human acceptor immunoglobulin and complementarity determining regions (CDR's) from a donor immunoglobulin capable of binding to an antigen, said method comprising the steps of substituting at least one human framework amino acids of the acceptor immunoglobulin with a corresponding amino acid from the donor immunoglobulin at a position in the immunoglobulins where:

(a) the amino acid is immediately adjacent to one of the CDR's; or

(b) the amino acid is predicted to have a side chain atom whose Van der Waals surface is within about 3Å of the CDR's in a three-dimensional immunoglobulin model and to be capable of interacting with the antigen or with the CDR's of the humanized immunoglobulin; with the proviso that when the chain is a heavy chain at least one of the substituted amino acids is capable of interacting with CDR's 2 or 3.

2. A method according to Claim 1, wherein the humanized immunoglobulin chain comprises in addition to the CDR's at least three amino acids from the donor immunoglobulin chosen by criteria (a) or (b).

3. A method of Claim 1, further comprising the prior step of comparing the framework or variable region amino acid sequence of the donor Ig with corresponding sequences in a collection of human Ig chains; and selecting to provide the human Ig framework one of the about three most homologous sequences from the collection.

4. A method according to Claim 3, wherein the human Ig framework sequence is selected from a collection of at least about ten Ig chain sequences.

5. An immunoglobulin comprising two light/heavy chain pairs, wherein at least one chain is designed in accordance with Claim 1.

6. An immunoglobulin according to Claim 1, which is specifically reactive with an antigen at an affinity of at least about 10^8 M^{-1} or stronger.

7. An immunoglobulin according to Claim 1, wherein the designed chain is a light chain comprising about 214 amino acids or a heavy chain comprising about 446 amino acids.

8. A DNA sequence which upon expression encodes a humanized immunoglobulin chain according to Claim 1.

9. A method for improving the affinity of a humanized immunoglobulin (Ig) to an antigen, by replacing amino acids of the human Ig framework with one to three or more amino acids from the donor Ig framework at positions where:

(a) the amino acid in the human framework region of the first immunoglobulin is rare for said position and the corresponding amino acid in the donor immunoglobulin is common for said position in human immunoglobulin sequences; or

(b) the amino acid is immediately adjacent to one of the CDR's; or

(c) the amino acid is predicted to have a side chain atom whose Van der Waals surface is within about 3Å of the CDR's in a three-dimensional immunoglobulin model and to be capable of interacting with the antigen or the CDR's of the humanized immunoglobulin.

10. A method according to Claim 9, wherein the additional amino acids comprise up to three amino acids,

each of which is immediately adjacent to one of the CDR's.

11. A method according to Claim 9, wherein the additional amino acids comprise at least two amino acids from the donor Ig which are predicted by modelling to be capable of interacting with the antigen or the CDR's.

12. A method according to Claim 9, wherein the humanized Ig has an affinity to the antigen within about 2 fold of the donor Ig.

13. A method of producing a humanized immunoglobulin containing a heavy chain and a light chain designed in accordance with Claim 9, said method comprising: culturing a host capable of expressing said heavy chain, said light chain, or both, under conditions suitable for production of said chains; and

recovering from the culture said humanized immunoglobulin.

14. A polynucleotide composition comprising a DNA sequence coding for a humanized immunoglobulin designed in accordance with Claim 9.

15. A method of producing an improved humanized immunoglobulin comprising expressing the polynucleotide composition of Claim 14.

16. A composition comprising a substantially pure humanized immunoglobulin capable of inhibiting binding of human interleukin-2 (IL-2) to a human IL-2 receptor.

17. A composition according to Claim 16, wherein the immunoglobulin exhibits a binding affinity to a human IL-2 receptor of about 10^8 M^{-1} or stronger.

18. A composition according to Claims 16, wherein the immunoglobulin comprises complementarity determining regions from one immunoglobulin and framework regions from at least one different immunoglobulin.

19. A recombinant immunoglobulin composition comprising a human framework and one or more foreign complementarity determining regions (CDRS) not naturally associated with the framework, wherein said immunoglobulin is capable of binding to a human interleukin-2 receptor.

20. A composition according to Claim 19, wherein all of the foreign CDR's are anti-Tac CDRs and the framework is an Eu immunoglobulin framework.

21. A composition according to Claim 19, wherein the immunoglobulin is an IgG_1 immunoglobulin isotype.

22. An immunoglobulin according to Claim 19, which is capable of blocking the binding of interleukin-2 (IL-2) to human IL-2 receptors.

23. An immunoglobulin according to Claim 19, wherein the human-like framework regions comprise amino acids sequences from at least two human immunoglobulins.

24. A method of treating T-cell mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of an immunoglobulin according to Claim 19.

25. A composition comprising a substantially pure humanized immunoglobulin specifically reactive with the p75 chain of the human IL-2 receptor.

26. A composition according to Claim 25, wherein the immunoglobulin exhibits a binding affinity to a human IL-2 receptor of about 10^7 M^{-1} or stronger.

27. A composition according to Claim 25, wherein the immunoglobulin comprises one or more foreign CDRs substantially homologous to a CDR from an immunoglobulin reactive with human p75 protein.

28. A composition according to Claim 25, wherein the immunoglobulin is capable of blocking the binding of interleukin-2 (IL-2) to the p75 chain of human IL-2 receptors.

29. A composition according to Claim 25, wherein the humanized immunoglobulin comprises the human framework regions having amino acids sequences from at least two human immunoglobulins.

30. A humanized immunoglobulin capable of binding to human interleukin-2 receptors, said immunoglobulin comprising one or more complementarity determining regions (CDR's) from mik-β1 antibody in a human framework.

31. A humanized immunoglobulin according to Claim 30, wherein the human framework is substantially homologous to an Lay immunoglobulin framework.

32. A humanized immunoglobulin according to Claim 30 which is capable of blocking the binding of IL-2 to interleukin-2 receptors on human T-cells.

33. A method of treating T-cell mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of an immunoglobulin according to Claim 30.

34. A humanized immunoglobulin according to Claim 30 which is complexed to a cytotoxic agent.

35. A composition comprising a substantially pure humanized immunoglobulin specifically reactive with a herpes simplex virus-specific epitope.

36. A composition according to claim 35, wherein the epitope is on a viral surface glycoprotein.

37. A composition according to claim 36, wherein the glycoprotein is gB or gD.

38. A composition comprising a substantially pure humanized immunoglobulin capable of inhibiting binding of a herpes simplex virus (HSV) protein to a mouse monoclonal antibody specifically reactive with said protein, wherein the humanized immunoglobulin comprises at least one complementarity determining region (CDR) from the mouse monoclonal antibody.

39. A composition according to Claim 38, wherein the humanized immunoglobulin exhibits a binding affinity of about 10^7 M^{-1} or stronger.

40. A composition according to Claim 38 wherein said immunoglobulin is capable of binding to type 1 or 2 herpes simplex virus (HSV).

41. A composition according to Claim 38, wherein the immunoglobulin comprises one or more CDR's substantially homologous to a CDR from an immunoglobulin reactive with HSV glycoprotein of gB, gD, gG or gH.

42. A composition according to Claim 38, wherein the immunoglobulin is an IgG_1 immunoglobulin isotype.

43. A humanized immunoglobulin capable of binding to herpes simplex virus, said immunoglobulin comprising one or more complementarity determining regions (CDR's) from a mouse monoclonal antibody in a human framework, wherein the mouse antibody is Fd 79 or Fd 138-80.

44. A humanized immunoglobulin according to Claim 43, wherein the human framework is substantially homologous to an Eu or a Pom immunoglobulin framework.

45. A humanized immunoglobulin according to Claim 43 which is capable of neutralizing HSV.

46. A method of treating herpes simplex virus mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of an immunoglobulin according to Claim 38.

47. A composition comprising a substantially pure humanized immunoglobulin specifically reactive with a CD33 antigen epitope.

48. A composition according to Claim 47, wherein a variable region of at least one chain of the immunoglobulin comprises three complementarity determining regions (CDR's) from a non-human antibody in a human framework.

49. A composition according to claim 48, wherein the chain is the heavy chain.

50. A composition according to claim 48, wherein the non-human antibody is M195.

51. A composition comprising a substantially pure humanized immunoglobulin capable of inhibiting

binding of CD33 antigen to a mouse monoclonal antibody specifically reactive with said antigen, wherein the humanized immunoglobulin comprises at least one complementarity determining region (CDR) from the mouse monoclonal antibody.

52. A composition according to Claim 51, wherein the humanized immunoglobulin exhibits a binding affinity of about 10^7 M^{-1} or stronger.

53. A composition according to Claim 51, which is capable of blocking the binding of mouse M195 antibody to human cells.

54. A composition according to Claim 51, wherein the humanized immunoglobulin comprises a human framework substantially homologous to Eu immunoglobulin framework.

55. A humanized immunoglobulin according to Claim 51 which is of capable mediating antibody-dependent cellular cytotoxicity in the presence of human target and effector cells.

56. A method of treating myeloid cell-mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of a composition according to Claim 51.

57. A composition according to claim 51, wherein the immunoglobulin is conjugated to a cytoxic agent.

58. A composition comprising a substantially pure humanized immunoglobulin specifically reactive with a human cytomegalovirus-specific epitope.

59. A composition according to Claim 58, wherein a variable region of at least one chain comprises three complementarity determining regions from a non-human immunoglobulin chain in a human framework.

60. A composition according to claim 58, wherein the epitope is on a viral surface glycoprotein.

61. A composition according to claim 60, wherein the glycoprotein is gB or gH.

62. A composition comprising a substantially pure humanized immunoglobulin capable of inhibiting binding of a cytomegalovirus (CMV) protein to a mouse monoclonal antibody specifically reactive with said protein, wherein the humanized immunoglobulin comprises at least one complementarity determining region (CDR) from the mouse monoclonal antibody.

63. A composition according to Claim 62, wherein the humanized immunoglobulin exhibits a binding affinity of about 10^7 M^{-1} or stronger.

64. A recombinant immunoglobulin composition comprising a human framework and one or more foreign complementarity determining regions (CDR's) not naturally associated with the framework, wherein said immunoglobulin is capable of binding to CMV.

65. A composition according to Claim 64, wherein all of the foreign CDR's are located on heavy chains of the immunoglobulin.

66. A composition according to Claim 64, wherein the immunoglobulin is an IgG_1 immunoglobulin isotype.

67. A composition according to Claim 64 wherein the immunoglobulin is capable of blocking the binding of CMV to human cells.

68. An immunoglobulin according to Claim 64, wherein the framework regions comprise amino acids sequences from at least two human immunoglobulins.

69. A humanized immunoglobulin capable of binding to cytomegalovirus, said immunoglobulin comprising one or more complementarity determining regions (CDR's) from a mouse monoclonal antibody in a human framework, wherein the mouse antibody is CMV5, CMV109 or CMV115.

70. A humanized immunoglobulin according to Claim 69, wherein the human framework is substantially homologous to an Eu or a Wol immunoglobulin framework.

71. A humanized immunoglobulin according to Claim 69 which is capable of neutralizing CMV.

72. A method of treating cytomegalovirus mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of an immunoglobulin according to Claim 69.

73. A method of treating cytomegalovirus mediated disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of a combination of two or more immunoglobulins according to Claims 69.

74. A composition comprising a substantially pure humanized immunoglobulin specifically reactive with human γ-IFN.

75. A composition according to Claim 74, wherein a variable region of at least one chain comprises three complementarity determining regions (CDR's) from a non-human antibody in a human framework.

76. A composition according to claim 75, wherein the non-human antibody is AF2.

77. A composition according to Claim 74 capable of inhibiting binding of human γ-IFN to a human γ-IFN receptor.

78. A recombinant immunoglobulin composition comprising a human framework and one or more complementarity determining regions (CDR's) not naturally associated with the framework, wherein said immunoglobulin is capable of specifically inhibiting biniding of human γ-IFN to a human γ-IFN receptor.

79. A composition according to Claim 78, wherein one or more of the foreign CDR's are substantially homologous to a CDR from the AF2 antibody.

80. A composition according to Claim 78, wherein the immunoglobulin is an IgG_1 immunoglobulin isotype.

81. A composition according to Claim 78, wherein the immunoglobulin is capable of blocking the binding of human γ-IFN antibody to human cells.

82. A method of treating autoimmune disorders in a human patient, said method comprising administering to said patient a therapeutically effective dose of a composition according to Claim 78.

83. A composition according to Claim 20, wherein the immunoglobulin is conjugated to a cytotoxic agent.

84. A composition according to Claim 35, wherein the immunoglobulin is conjugated to a cytotoxic agent.

85. A composition according to Claim 64, wherein the immunoglobulin is conjugated to a cytotoxic agent.